IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

OSBORNE et al. Atty. Ref.: 620-412; Confirmation No. 4519

Appl. No. 10/567,453 TC/A.U. 1633

Filed: February 7, 2006 Examiner: Marvich

For: MYELOMA CELL CULTURE IN TRANSFERRIN-FREE LOW IRON MEDIUM

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October 13, 2011

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REQUEST FOR NEW ACTION AND CONSIDERATION OF EVIDENCE OF RECORD

The Office Action of October 5, 2011 in the above has been obtained from the PTO IFW.

A new Action is requested, with the date for response re-set from the mailing of the new Action, and withdrawal of the Office Action of October 5, 2011, as the Office Action of October 5, 2011 fails to consider the Declaration evidence filed July 6, 2011 (Declaration of Non-Obviousness Under 37 C.F.R. s103 of Raymond Field).

The Advisory Action of July 22, 2011 stated that the Declaration would not be entered "because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented." See box 8. of the Advisory Action.

The RCE filed September 2, 2011 specifically requested consideration of the reply of July 6, 2011 and the "Field Declaration filed July 6, 2011". A specific request for consideration of the Declaration should not have been required.

In not considering the earlier presented evidence, the Office Action of October 5, 2011 is incomplete and a new Action is requested with the date re-set from the mailing of the new Action.

The applicants note that Rule 104 provides the following requirement for completeness of Office Actions:

> (a) Examiner's action.
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> (1) On taking up an application for examination or a patent in a reexamination proceeding, the examiner shall make a thorough study thereof and shall make a thorough investigation of the available prior art relating to the subject matter of the claimed invention. The examination shall be complete with respect both to compliance of the application or patent under reexamination with the applicable statutes and rules and to the patentability of the invention as claimed, as well as with respect to matters of form, unless otherwise indicated.
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> (2) The applicant, or in the case of a reexamination proceeding, both the patent owner and the requester, will be notified of the examiner's action. The reasons for any adverse action or any objection or requirement will be stated in an Office action and such information or references will be given as may be useful in aiding the applicant, or in the case of a reexamination proceeding the patent owner, to judge the propriety of continuing the prosecution. ...
>
> (b) Completeness of examiner's action. The examiner's action will be complete as to all matters, except that in appropriate circumstances, such as misjoinder of invention, fundamental defects in the application, and the like, the action of the examiner may be limited to such matters before

> further action is made. However, matters of form need not be raised by the examiner until a claim is found allowable.

MPEP § 716.01(B) confirms that "evidence traversing rejections, when timely presented, must be considered by the examiner whenever present." Specifically, the MPEP section provides the following:

> "All entered affidavits, declarations, and other evidence traversing rejections are acknowledged and commented upon by the examiner in the next succeeding action. The extent of the commentary depends on the action taken by the examiner. Where an examiner holds that the evidence is sufficient to overcome the prima facie case, the comments should be consistent with the guidelines for statements of reasons for allowance. See MPEP § 1302.14. Where the evidence is insufficient to overcome the rejection, the examiner must specifically explain why the evidence is insufficient. General statements such as "the declaration lacks technical validity" or "the evidence is not commensurate with the scope of the claims" without an explanation supporting such findings are insufficient."

A new Office Action which includes consideration of the previously-filed and entered Declaration evidence is requested, with the date for responding being re-set from the mail date of the new Action.

The applicants note that the Examiner's comments in the Office Action of October 5, 2011 appear to rely on assertions similar to those raised in the Advisory Action of July 22, 2011 wherein the Examiner asserted that "Fields et al [U.S. Patent No. 6,593,140[1]] teaches the FAC can serve as an iron chelator in growth of myeloma cells." See also page 7 of the Office Action dated October 5, 2011 ("Specifically, Fields

[1] The inventor of U.S. Patent No. 6,593,140 is Raymond Paul Field, who is also the Declarant of the Declaration filed July 6, 2011.

et al teach the use of FAC as an iron chelator for growth of cells including myeloma cells….. Fields et al teaches use of FAC in growth methods.").

The evidence presented in the Field Declaration discusses the disclosure of the cited art and explains that while Figure 2A of the cited Field patent shows that high concentrations of iron in the culture medium are required in order to transport iron into hybridoma cells in culture in static flasks in the absence of either transferring or lipophilic iron chelator (e.g. tropolone), in cultures of hybridoma cells that are shaken or agitated (to simulate a fermenter/bioreactor environment) it was shown by Field that for some hybridomas, high iron concentrations in the absence of transferring or a chelator resulted in cell death. Field states that Figure 2B of his patent demonstrates this resulting cell death. Field explains in the Declaration filed July 6, 2011 that these results were the basis for the use by the Field patent of tropolone to supply iron to the hybridoma and other cells in culture by only using a low iron concentration.

Field goes on to explain in the Declaration filed July 6, 2011 that it was surprising and unexpected that although hybridoma cells – which are a fusion of a myeloma cell and a B lymphocyte – are destroyed by higher levels of iron supplied as Ferric Ammonium Citrate (FAC) in agitated suspension culture in the absence of transferring or a chelator (as taught by Field), myeloma cells – which are one fusion partner of a hybridoma – can thrive and grow with the same iron levels under similar conditions, as demonstrated in the present application. Field explains, for example, that this was surprising since hybridoma cells and myeloma cells in all other aspects of

culture process parameters behave essentially identically to each other; and often differently to many other cell types, such as CHO cells.

In the Advisory Action of July 22, 2011, the Examiner asserts that the basis for the rejection is that Gorfien teaches the instant method, but does not provide details of the iron chelator. The Examiner turns to Field, where allegedly FAC is taught as an iron chelator for growth of myeloma cells. This is factually incorrect as Field emphatically does not illustrate *growth* of myeloma cells. Field very clearly teaches away from the use of FAC for *growth* of cells as evidenced by Example 5 of Field "myeloma cells failed to thrive and died within 48 hours". Failure to thrive is clearly the opposite of *growth*.

Contrary to the Examiner's statement that "One would looking at the methods of Gorfien et al be motivated to sue FAC as Gorfien et al directs one to ferric citrate chelators in the methods of growing myeloma cells " [sic], a skilled artisan would not contemplate using FAC as described in Field in the method of Gorfien because Field clearly shows in Example 5 that myeloma cells grown using FAC did not grow.

The Examiner states that "The failures of Fields et al are not demonstrated to be due to use of FAC but most presumably by differences in the methods of Fields et al and Gorfien et al." It is not apparent how the Examiner arrives at this conclusion. Field et al demonstrate that myeloma cells do not grow in the presence of FAC and the absence of transferrin. This demonstration is in agreement with the whole body of art available at the time, as discussed in previous responses. Gorfien does not provide any results at all on the ability of myeloma cells to grow when ferric citrates replace transferrin. The Examiner is incorrect to say that Fields' failure and Gorfien's success is

due to different methods when Gorfien does not demonstrate successful growth but Field does demonstrate failure to grow.

Furthermore, Figure 2b of Field shows no growth of hybridoma cells in shaking T-flask cultures where FAC is used as the iron source in the absence of transferrin. This example demonstrates that the higher the concentration of FAC used, the less number of cells are viable. This is a clear teaching away from the use of FAC and cannot be dismissed based on the Examiner's assertion that the failure of growth in Field is due to the difference in the methods of Gorfien and Field. If the skilled person took the teaching of Field into account, he would be taught that FAC does not support growth of myeloma or hybridoma cells in the absence of transferrin, and that increasing the concentration of FAC reduces the viability of hybridoma cells even further (no equivalent data is shown or discussed for myeloma cells). The person skilled in the art would have to go against that teaching and attempt to use FAC in combination with the methods of Gorfien. This clearly demonstrates inventive activity on behalf of the inventors.

The cited combination of art provides no reasonable expectation that the presently claimed method would be achievable. The results of Field would deter the skilled artisan from using FAC when attempting to grow myeloma cells in the absence of transferrin.

Consideration of the entirety of the previously filed evidence, and a new Action or Notice of Allowance are requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required to place the application in condition for allowance.

The undersigned telephoned and left the Examiner a message on October 6, 2011 requesting the opportunity to discuss the Office Action of October 5, 2011. The undersigned spoke by telephone with the Examiner on October 11, 2011, and requested a new Action. The undersigned requested the Examiner's advice as to whether a written request, such as this paper, was required and it was the undersigned's understanding that the Examiner would consider the matter with the Examiner's Supervisor and return to the undersigned with a recommendation. To date, the undersigned has not received the Examiner's further recommendations.

A new Action with the date re-set for responding from the mail date of the new Action, which considers the above and the evidence of record, are requested.

Respectfully submitted,

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